NMCP COVID-19 Literature Report #40: Friday, 18 September 2020

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Purpose: These now weekly reports, published on Fridays, are curated collections of current research, evidence reviews, and news regarding the COVID-19 pandemic. Please feel free to reach out with questions, suggestions for future topics, or any other concerns.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily.

Statistics

Global today: 30,217,420 confirmed cases and 946,847 deaths in 188 countries/regions

7 days ago: 28,212,036 confirmed cases and 910,314 deaths in 188 countries/regions

14 days ago: 26,347,573 confirmed cases and 869,600 deaths in 188 countries/regions

United States*

top 5 states by cases (Virginia is ranked 15th)

	TOTAL US	CA	TX	FL	NY	GA
Confirmed Cases	6,677,516	775,679	701,350	674,456	447,262	300,903
Tests	91,546,598	13,080,037	5,345,176	5,010,973	9,621,920	2,679,891
Deaths	197,682	14,826	14,826	13,086	33,070	6,474

^{*}see <u>census.gov</u> for current US Population data; NA: not all data available

JHU CSSE as of 1000 EDT 18 September 2020

Virginia	Total	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	138,702	4,169	1,761	2,638	4,721	2,500	1,885	6,596
Hospitalized	10,520	382	58	90	346	268	123	354
Deaths	2,949	66	21	32	67	49	70	78

VA DOH as of 1000 EDT 18 September 2020

Special Reports

OWS: <u>Operation Warp Speed Strategy for Distributing a COVID-19 Vaccine [pdf]</u> (published 16 September 2020)

"The U.S. Department of Health and Human Services (HHS) and Department of Defense (DoD) today released two documents outlining the Trump Administration's detailed strategy to deliver safe and effective COVID-19 vaccine doses to the American people as quickly and reliably as possible.

The documents, developed by HHS in coordination with DoD and the Centers for Disease Control and Prevention (CDC), provide a strategic distribution overview along with an interim playbook for state, tribal, territorial, and local public health programs and their partners on how to plan and operationalize a vaccination response to COVID-19 within their respective jurisdictions....

The strategic overview lays out four tasks necessary for the COVID-19 vaccine program:

- Engage with state, tribal, territorial, and local partners, other stakeholders, and the
 public to communicate public health information around the vaccine and promote
 vaccine confidence and uptake.
- Distribute vaccines immediately upon granting of Emergency Use Authorization/ Biologics License Application and once CDC has made vaccine recommendations, using a transparently developed, phased allocation methodology.
- Ensure safe administration of the vaccine and availability of administration supplies.
- Monitor necessary data from the vaccination program through an information technology (IT) system capable of supporting and tracking distribution, administration, and other necessary data." (DOD)

See also: COVID-19 vaccination program playbook [pdf] and distribution infographic [pdf]

GPMB: A world in disorder (published 14 September 2020)

"In this report, the GPMB [Global Preparedness Monitoring Board] provides a harsh assessment of the global COVID-19 response, warning that the world cannot afford to be unprepared again when the next pandemic hits. The Board called for five urgent actions to be taken to bring order out of the catastrophe and chaos currently facing the world: responsible leadership; engaged citizenship; strong and agile systems for health security; sustained investment; and robust global governance of preparedness."

AAP: <u>Caring for Children and Youth With Special Health Care Needs During the COVID-19</u> Pandemic (updated 01 September 2020)

"This web page discusses the overall approach to minimizing the risk of infection while meeting the ongoing needs of children and youth with special health care needs during the COVID-19 pandemic."

Gates Foundation: COVID-19: A Global Perspective (September 2020)

"In past editions of the Goalkeepers Report—almost every time we have opened our mouths or put pen to paper, in fact—we have celebrated decades of historic progress in fighting poverty and disease.

But we have to confront the current reality with candor: This progress has now stopped. In this report, we track 18 indicators included in the United Nations' Sustainable Development Goals (SDGs). In recent years, the world has improved on every single one. This year, on the vast majority, we've regressed.

And so this essay has two goals. First, we analyze the damage the pandemic has done and is still doing—to health, to economies, and to virtually everything else. Second, we argue for a collaborative response. There is no such thing as a national solution to a global crisis. All countries must work together to end the pandemic and begin rebuilding economies. The longer it takes us to realize that, the longer it will take (and the more it will cost) to get back on our feet."

Selected Literature: Peer-Reviewed Journals

Date given is the date published or posted online; often these papers are ahead of print.

17 September 2020

JAMA: <u>Change in Antibodies to SARS-CoV-2 Over 60 Days Among Health Care Personnel in</u> Nashville, Tennessee

"Anti–SARS-CoV-2 antibodies to the spike protein, which have correlated with neutralizing antibodies, decreased over 60 days in health care personnel, with 58% of seropositive individuals becoming seronegative. The consistency in decline in the signal-to-threshold ratio regardless of the baseline ratio and a higher proportion of asymptomatic participants becoming seronegative support the interpretation as a true decline over a 2-month period rather than an artifact of assay performance. If replicated, these results suggest that cross-sectional seroprevalence studies to evaluate population immunity may underestimate rates

of prior infections because antibodies may only be transiently detectable following infection.

The window after recovering from SARS-CoV-2 infection when people could donate serum that has sufficiently high antibody levels may be limited."

16 September 2020

MMWR: <u>Characteristics and Maternal and Birth Outcomes of Hospitalized Pregnant Women</u> with Laboratory-Confirmed COVID-19 — <u>COVID-NET</u>, 13 States, <u>March 1</u>—August 22, 2020

"Information on the clinical characteristics and birth outcomes of hospitalized U.S. pregnant women with COVID-19 is limited.

Among 598 hospitalized pregnant women with COVID-19, 55% were asymptomatic at admission. Severe illness occurred among symptomatic pregnant women, including intensive care unit admissions (16%), mechanical ventilation (8%), and death (1%). Pregnancy losses occurred for 2% of pregnancies completed during COVID-19-associated hospitalizations and were experienced by both symptomatic and asymptomatic women.

Pregnant women and health care providers should be aware of potential risks for severe COVID-19, including adverse pregnancy outcomes. Identifying COVID-19 during birth hospitalizations is important to guide preventive measures to protect pregnant women, parents, newborns, other patients, and hospital personnel."



MMWR: <u>SARS-CoV-2 Infection Among Hospitalized Pregnant Women: Reasons for Admission and Pregnancy Characteristics — Eight U.S. Health Care Centers, March 1—May 30, 2020</u>

"Prevalences of prepregnancy obesity and gestational diabetes were higher among pregnant women hospitalized for COVID-19—related illness (e.g., worsening respiratory status) than among those admitted for pregnancy-related treatment or procedures (e.g., delivery) and found to have COVID-19. Intensive care was required for 30% (13 of 43) of pregnant women admitted for COVID-19, and one pregnant woman died from COVID-19.

Antenatal counseling emphasizing preventive measures, including use of masks, frequent hand washing, and social distancing, might help prevent COVID-19 among pregnant women, especially those with prepregnancy obesity and gestational diabetes."

15 September 2020

Int J Infect Dis: Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients

"Highlights:

- Viable (infectious) SARS-CoV-2 was present in aerosols within the hospital room of COVID-19 patients.
- Airborne virus was detected in the absence of health-care aerosol-generating procedures.
- The virus strain detected in the aerosols matched the virus strain isolated from a patient with acute COVID-19."

Previously posted on 04 August 2020 to medRxiv:

https://www.medrxiv.org/content/10.1101/2020.08.03.20167395v1

MMWR: <u>SARS-CoV-2</u>—<u>Associated Deaths Among Persons Aged <21 Years — United States,</u> February 12–July 31, 2020

"Among 121 SARS-CoV-2—associated deaths among persons aged <21 years reported to CDC by July 31, 2020, 12 (10%) were infants and 85 (70%) were aged 10—20 years. Hispanic, non-Hispanic Black and non-Hispanic American Indian/Alaskan Native persons accounted for 94 (78%) of these deaths; 33% of deaths occurred outside of a hospital.

Persons aged <21 years exposed to SARS-CoV-2 should be monitored for complications. Ongoing surveillance for SARS-CoV-2—associated infection, hospitalization, and death among persons aged <21 years should be continued as schools reopen in the United States."

Am J Trop Med Hyg: Stability of SARS-CoV-2 on Produce following a Low-Dose Aerosol Exposure

"We modeled the stability of SARS-CoV-2 on apples, tomatoes, and jalapeño peppers at two temperatures following a low-dose aerosol exposure designed to simulate an airborne transmission event involving droplet nuclei. Infectious virus was not recovered postexposure."

EClinicalMedicine: <u>Tracing asymptomatic SARS-CoV-2 carriers among 3674 hospital staff: a cross-sectional survey</u>

"In our hospital, all hospital staff have received throat swab RT-PCR test, plasma COVID-19 IgM/IgG antibodies test and chest CT examination. We analyzed the correlation between infection rates and gender, age, job position, work place and COVID-19 knowledge training of the staff. After that, all asymptomatic staff were re-examined weekly for 3 weeks.

A total of 3764 hospital staff were included in this single-center cross-sectional study. Among them, 126 hospital staff had abnormal findings, and the proportion of asymptomatic infection accounted for 0.76% (28/3674). There were 26 staff with IgM+, 73 with IgG+, and 40 with ground glass shadow of chest CT. Of all staff with abnormal findings, the older they are, the more likely they are to be the staff with abnormal results, regardless of their gender. Of 3674 hospital staff, the positive rate of labor staff is obviously higher than that of health care workers (HCWs) and administrative staff (P<0.05). In the course of participating in the treatment of COVID-19, there was no statistically significant difference in positive rates between high-risk departments and low-risk departments (P>0.05). The positive rate of HCWs who participated in the COVID-19 knowledge training was lower than those did not participate in early training (P <0.01). Importantly, it was found that there was no statistical difference between the titers of IgM antibody of asymptomatic infections and confirmed patients with COVID-19 in recovery period (P>0.05). During 3 weeks follow-up, all asymptomatic patients did not present the development of clinical symptoms or radiographic abnormalities after active intervention in isolation point.

To ensure the safety of resumption of work, institutions should conduct COVID-19 prevention training for staff and screening for asymptomatic patients, and take quarantine measures as soon as possible in areas with high density of population."

J Pediatr Infect Dis: <u>The Natural History of SARS-Cov-2 Related Multisystem Inflammatory</u> <u>Syndrome in Children (MIS-C): A Systematic Review</u>

"The clinical manifestations and natural history of severe acute respiratory distress syndrome coronavirus 2 (SARS-Cov-2) related Multisystem Inflammatory Syndrome in Children (MIS-C) are poorly defined. Using a systematic review of individual cases and case series and collating elements of the clinical course, the objective of this study was to provide a detailed clinical description and natural history of MIS-C....

MEDLINE and EMBASE searches produced 129 articles and 10 articles were identified from journal contents or article bibliographies; 16 reports describing 505 children with MIS-C comprise this review. Thirty-two children (14.7%) had negative results for SARS-Cov-2 by nucleic acid and/or antibody testing. The weighted median age was 9 years (6 months to 20 years). Clinical findings included fever (100%), gastrointestinal symptoms (88.0%), rash (59.2%), conjunctivitis (50.0%), chelitis/ "strawberry tongue" (55.7%) or extremity edema/erythema (47.5%). Median serum CRP, ferritin, fibrinogen and D dimer concentrations were above the normal range. Intravenous gammaglobulin (78.1%) and methylprednisolone/prednisone(57.6%) were the most common therapeutic interventions; immunomodulation was used in 24.3% of cases. Myocardial dysfunction requiring ionotropic support (57.4%) plus extracorporeal membrane oxygenation (5.3%), respiratory distress requiring mechanical ventilation (26.1%), and acute kidney injury (11.9%) were the major complications; anticoagulation was used commonly (54.4%) but thrombotic events occurred rarely (3.5%). Seven (1.4%) children died.

MIS-C following SARS-Cov-2 infection frequently presents with gastrointestinal complaints and/or rash; conjunctivitis, chelitis and/or extremity changes also occur frequently. Serious complications occur frequently and respond to aggressive supportive therapy."

JAMA Pediatr: <u>Frequency of Children vs Adults Carrying Severe Acute Respiratory Syndrome</u> <u>Coronavirus 2 Asymptomatically</u>

"In this study conducted among individuals hospitalized in Milan, one of the cities with the highest SARS-CoV-2 burden in the world, about 1% of children and 9% of adults without any symptoms or signs of SARS-CoV-2 infection tested positive for the virus. It has been estimated that approximately 80% of adults with SARS-CoV-2 are asymptomatic. The few available reports on children are from China and suggest that children who are asymptomatic might be 15% of individuals positive for SARS-CoV-2. In this study, children without symptoms and signs of SARS-CoV-2 carried the virus less frequently than adults, suggesting that their role as facilitators of the spreading of SARS-CoV-2 infection could be reconsidered."

Mol Psychiatr: <u>COVID-19 risk and outcomes in patients with substance use disorders: analyses from electronic health records in the United States</u>

"The global pandemic of COVID-19 is colliding with the epidemic of opioid use disorders (OUD) and other substance use disorders (SUD) in the United States (US). Currently, there is limited data on risks, disparity, and outcomes for COVID-19 in individuals suffering from SUD. This is a retrospective case-control study of electronic health records (EHRs) data of 73,099,850 unique patients, of whom 12,030 had a diagnosis of COVID-19. Patients with a recent diagnosis of SUD (within past year) were at significantly increased risk for COVID-19 (adjusted odds ratio or AOR = 8.699 [8.411-8.997], $P < 10^{-30}$), an effect that was strongest for individuals with OUD (AOR = 10.244 [9.107-11.524], $P < 10^{-30}$), followed by individuals

with tobacco use disorder (TUD) (AOR = 8.222 ([7.925-8.530], P < 10^{-30}). Compared to patients without SUD, patients with SUD had significantly higher prevalence of chronic kidney, liver, lung diseases, cardiovascular diseases, type 2 diabetes, obesity and cancer. Among patients with recent diagnosis of SUD, African Americans had significantly higher risk of COVID-19 than Caucasians (AOR = 2.173 [2.01-2.349], P < 10^{-30}), with strongest effect for OUD (AOR = 4.162 [3.13-5.533], P < 10^{-25}). COVID-19 patients with SUD had significantly worse outcomes (death: 9.6%, hospitalization: 41.0%) than general COVID-19 patients (death: 6.6%, hospitalization: 30.1%) and African Americans with COVID-19 and SUD had worse outcomes (death: 13.0%, hospitalization: 50.7%) than Caucasians (death: 8.6%, hospitalization: 35.2%). These findings identify individuals with SUD, especially individuals with OUD and African Americans, as having increased risk for COVID-19 and its adverse outcomes, highlighting the need to screen and treat individuals with SUD as part of the strategy to control the pandemic while ensuring no disparities in access to healthcare support."

12 September 2020

J Med Virol: Efficacy of Tocilizumab in COVID-19: A Systematic review and Meta-Analysis

"The efficacy of tocilizumab (TOC), monoclonal antibody against Interleukin-6 (IL-6) receptor, in patients with Coronavirus disease-2019 (COVID-19) patients has led to conflicting results. We performed a systematic review and meta-analysis to compare the efficacy of addition of TOC to standard of care (SOC) versus SOC in patients with COVID-19.

We performed a comprehensive literature search of PubMed, Embase, Web of Science, WHO COVID, LitCOVID and Cochrane databases. Pooled outcomes (overall mortality, need for mechanical ventilation, intensive care unit (ICU) admission, and secondary infections) were compared using DerSimonian-Laird/Random-effects approach. Risk difference (RD), confidence interval (CI), and p-values were generated.

A total of 23 studies with 6279 patients (1897 in TOC and 4382 in SOC group, respectively) were included. The overall mortality was lower in TOC group compared to SOC group (RD: -0.06, CI: -0.12 - -0.01, p = 0.03). Subgroup analysis including studies with only severe cases revealed lower mortality (RD: -0.12, CI: -0.18 - -0.06, p <0.01) and need for mechanical ventilation (RD: -0.11, CI: -0.19 - -0.02, p = 0.01) in TOC group compared to SOC group.

The addition of TOC to SOC has the potential to reduce mortality and need for mechanical ventilation in patients with severe COVID-19. Randomized controlled trials are needed to validate this."

J Pediatr Infect Dis: <u>Multicenter interim guidance on use of antivirals for children with COVID-</u> 19/SARS-CoV-2

"A panel of pediatric infectious diseases physicians and pharmacists from 20 geographically diverse North American institutions was convened. Through a series of teleconferences and web-based surveys, a set of guidance statements was developed and refined based on review of the best available evidence and expert opinion.

Given the typically mild course of COVID-19 in children, supportive care alone is suggested for most cases. For children with severe illness, defined as a supplemental oxygen requirement without need for non-invasive or invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO), remdesivir is suggested, preferably as part of a clinical trial if available. Remdesivir should also be considered for critically ill children requiring invasive or non-invasive mechanical ventilation or ECMO. A duration of 5 days is appropriate for most patients. The panel recommends against the use of hydroxychloroquine or lopinavir-ritonavir (or other protease inhibitors) for COVID-19 in children.

Antiviral therapy for COVID-19 is not necessary for the great majority of pediatric patients. For children with severe or critical disease, this guidance offers an approach for decision-making regarding use of remdesivir."

J Pediatr Infect Dis: <u>Heavy exposure of children aged 9 to 12 years with SARS-CoV-2 did not lead to infection</u>

"The reason for the apparently lower infection rate of children with SARS-CoV-2 compared to adults is still unclear. Here, we report on four school children with heavy exposure to SARS-CoV-2 with no clinical signs of COVID-19, repeated negative nasopharyngeal swabs for SARS-CoV-2 RNA, and no seroconversion."

11 September 2020

Ann Intern Med: Every Body Counts: Measuring Mortality From the COVID-19 Pandemic

"As of mid-August 2020, more than 170 000 U.S. residents have died of coronavirus disease 2019 (COVID-19); however, the true number of deaths resulting from COVID-19, both directly and indirectly, is likely to be much higher. The proper attribution of deaths to this pandemic has a range of societal, legal, mortuary, and public health consequences. This article discusses the current difficulties of disaster death attribution and describes the strengths and limitations of relying on death counts from death certificates, estimations of indirect deaths, and estimations of excess mortality. Improving the tabulation of direct and indirect deaths on death certificates will require concerted efforts and consensus across medical institutions and public health agencies. In addition, actionable estimates of excess

mortality will require timely access to standardized and structured vital registry data, which should be shared directly at the state level to ensure rapid response for local governments. Correct attribution of direct and indirect deaths and estimation of excess mortality are complementary goals that are critical to our understanding of the pandemic and its effect on human life."

Clin Infect Dis: <u>Social Disadvantage</u>, <u>Politics</u>, and <u>SARS-CoV-2 Trends</u>: <u>A County-Level Analysis of</u> United States Data

"We conducted a retrospective analysis of the relationship between the change in reported SARS-CoV-2 case counts at the US county level during June 1, 2020 – June 30,2020 and social, demographic, and political characteristics of the county.

1023/3142 US counties were included in the analysis. 678 (66·3%) had increasing, and 345 (33·7%) had non-increasing SARS-CoV-2 case counts between June 1 – June 30, 2020. In bivariate analysis, counties with increasing case counts had significantly higher Social Deprivation Index (median 48, IQR 24 – 72) than counties with non-increasing case counts (median 40, IQR 19 – 66; p=0·009). Counties with increasing case counts were significantly more likely to be metropolitan areas of 250,000 – 1 million population (p&0·001), to have a higher percentage of Black residents (9% vs. 6%, p=0·013), and to have voted for the Republican presidential candidate in 2016 by a 10-point or greater margin (p=0·044). In the multivariable model, metropolitan areas of 250,000 – 1 million population, higher percentage of Black residents and a 10-point or greater Republican victory were independently associated with increasing case counts.

Increasing case counts of SARS-CoV-2 in the US during June 2020 were associated with a combination of sociodemographic and political factors. Addressing social disadvantage and differential belief systems that may correspond with political alignment will play a critical role in pandemic control."

J Dent Res: Oral Manifestations in Patients with COVID-19: A Living Systematic Review

"This living systematic review aims to summarize evidence on the prevalence of oral signs and symptoms in patients with COVID-19. The review was reported per the PRISMA checklist, and the literature search was conducted in 6 databases and in gray literature. Studies published in any language mentioning oral symptoms and signs in patients with COVID-19 were included. The risk of bias was assessed by the Joanna Briggs Institute appraisal tools. The certainty of evidence was evaluated through GRADE assessment. After a 2-step selection, 40 studies were included: 33 cross-sectional and 7 case reports. Overall, 10,228 patients (4,288 males, 5,770 females, and 170 unknown) from 19 countries were assessed. Gustatory impairment was the most common oral manifestation, with a prevalence of 45% (95% CI, 34% to 55%; I2 = 99%). The pooled eligible data for different taste disorders were 38% for dysgeusia and 35% for hypogeusia, while ageusia had a prevalence of 24%. Taste disorders were associated with COVID-19 (odds ratio [OR], 12.68;

95% CI, 6.41 to 25.10; I2 = 63%; P < 0.00001), mild/moderate severity (OR, 2.09; 95% CI, 1.25 to 3.49; I2 = 66%; P = 0.005), and female patients (OR, 1.64; 95% CI, 1.23 to 2.17; I2 = 70%; P = 0.0007). Oral mucosal lesions presented multiple clinical aspects, including white and erythematous plaques, irregular ulcers, small blisters, petechiae, and desquamative gingivitis. Tongue, palate, lips, gingiva, and buccal mucosa were affected. In mild cases, oral mucosal lesions developed before or at the same time as the initial respiratory symptoms; however, in those who required medication and hospitalization, the lesions developed approximately 7 to 24 d after onset symptoms. Therefore, taste disorders may be common symptoms in patients with COVID-19 and should be considered in the scope of the disease's onset and progression. Oral mucosal lesions are more likely to present as coinfections and secondary manifestations with multiple clinical aspects."

JAMA Cardiol: <u>Cardiovascular Magnetic Resonance Findings in Competitive Athletes Recovering</u>
From COVID-19 Infection

"Of 26 competitive athletes, 4 (15%) had CMR findings suggestive of myocarditis and 8 additional athletes (30.8%) exhibited LGE without T2 elevation suggestive of prior myocardial injury. COVID-19—related myocardial injury in competitive athletes and sports participation remains unclear. Cardiac magnetic resonance imaging has the potential to identify a high-risk cohort for adverse outcomes and may, importantly, risk stratify athletes for safe participation because CMR mapping techniques have a high negative predictive value to rule out myocarditis. A recent study by Puntmann et al demonstrated cardiac involvement in a significant number of patients who had recovered from COVID-19. A recent expert consensus article recommended 2-week convalescence followed by no diagnostic cardiac testing if asymptomatic and an electrocardiogram and transthoracic echocardiogram in mildly symptomatic athletes with COVID-19 to return to play for competitive sports. However, emerging knowledge and CMR observations question this recommendation. Cardiac magnetic resonance imaging evidence of myocardial inflammation has been associated with poor outcomes, including myocardial dysfunction and mortality."

PLoS One: Relationship quality and mental health during COVID-19 lockdown

"Catastrophes are known to have an impact on relationships as well as on mental health. This study evaluated differences in several mental health and well-being measures according to relationship quality during the Coronavirus Disease (COVID-19) pandemic and related lockdown measures. A cross-sectional online survey was launched four weeks after lockdown measures were implemented in Austria. Relationship quality was measured with the Quality of Marriage Index (QMI), and mental health measures included quality of life (WHO-QOL BREF psychological domain), well-being (WHO-5), depression (PHQ-9), anxiety (GAD-7), stress (PSS-10), and sleep quality (ISI). ANOVAs with Bonferroni-corrected post-hoc tests and Chisquared tests were applied. In all mental health scales, individuals with good relationship quality (n = 543) scored better than individuals with poor relationship quality (n

= 190) or without relationship (n = 272). The odds ratios (OR) between the poor and good relationship quality groups were 3.5 for the PHQ-9, 3.4 for the GAD-7, and 2.0 for the ISI. Additionally, individuals without no relationship scored better on all scales than individuals with poor relationship quality (all p-values < .05). Relationship quality was related to mental health during COVID-19. The prevalence of depressive symptoms increased according to relationship quality from 13% up to 35%. Relationship per se was not associated with better mental health, but the quality of the relationship was essential. Compared to no relationship, a good relationship quality was a protective factor whereas a poor relationship quality was a risk factor."

10 September 2020

Eurosurveill: Reduced maximal aerobic capacity after COVID-19 in young adult recruits, Switzerland, May 2020

"The 2019 coronavirus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged as a pandemic in late 2019, and is ongoing at the time of writing. Long-term sequelae of COVID-19 are still unknown. Pulmonary sequelae impairing physical fitness have been described predominantly for hospitalised patients with COVID-19. Although lung lesions have also been described in asymptomatically infected individuals, it is yet unclear if these observations correlate with a measurable functional deficit in physical fitness. We performed a well-established and validated physical fitness test before and after an outbreak of COVID-19 among young adult Swiss recruits. By measuring the change in predicted maximal aerobic capacity (VO2 max) of not infected, asymptomatically infected and convalescent COVID-19 individuals, we found a decrease in VO2 max among COVID-19 convalescent but not among asymptomatically and not infected recruits."

Eurosurveill: <u>Transmission of SARS-CoV-2 in children aged 0 to 19 years in childcare facilities</u> and schools after their reopening in May 2020, Baden-Württemberg, <u>Germany</u>

"To gain further understanding on paediatric transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the school/childcare-facility context, we compiled and analysed data from SARS-CoV-2 infected children (age: 0–19 years), who had been to school/childcare facilities, after such establishments reopened in Baden-Württemberg in May 2020....

Our investigation suggests that child-to-child transmission in schools and childcare facilities is uncommon and not the primary cause of SARS-CoV-2 infection in children. Based on our estimation there could be one secondary case per roughly 25 infectious school days. This ratio of 1 in 25 might, however, overestimate the transmission risk in schools and childcare facilities, because some of the 104 index cases (i.e. 104 = 557 - 453) for whom no

information on school attendance was available, may also have spent some time in school or in a childcare facility while being infectious, yet without further generating any notified COVID-19 cases."

NEJM: <u>Rapid Scaling Up of Covid-19 Diagnostic Testing in the United States — The NIH RADx</u> Initiative

"In this article, we describe the additional role of the NIH in the effort to increase the range and availability of diagnostic tests for the causative virus, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2)."

PLoS Pathog: <u>A comprehensive</u>, <u>longitudinal analysis of humoral responses specific to four recombinant antigens of SARS-CoV-2 in severe and non-severe COVID-19 patients</u>

"There is an urgent need for effective treatment and preventive vaccine to contain this devastating global pandemic, which requires a comprehensive understanding of humoral responses specific to SARS-CoV-2 during the disease progression and convalescent phase of COVID-19 patients. We continuously monitored the serum IgM and IgG responses specific to four SARS-CoV-2 related antigens, including the nucleoprotein (NP), receptor binding domain (RBD), S1 protein, and ectodomain (ECD) of the spike protein among non-severe and severe COVID-19 patients for seven weeks since disease onset. Most patients generated humoral responses against NP and spike protein-related antigens but with their distinct kinetics profiles. Combined detection of NP and ECD antigens as detecting antigen synergistically improved the sensitivity of the serological assay, compared to that of using NP or RBD as detection antigen. 80.7% of convalescent sera from COVID-19 patients revealed that the varying extents of neutralization activities against SARS-CoV-2. S1-specific and ECD-specific IgA responses were strongly correlated with the neutralization activities in non-severe patients, but not in severe patients. Moreover, the neutralizing activities of the convalescent sera were shown to significantly decline during the period between 21 days to 28 days after hospital discharge, accompanied by a substantial drop in RBD-specific IgA response. Our data provide evidence that are crucial for serological testing, antibody-based intervention, and vaccine design of COVID-19."

Science: Cryptic transmission of SARS-CoV-2 in Washington state

"Following its emergence in Wuhan, China, in late November or early December 2019, the SARS-CoV-2 virus has rapidly spread globally. Genome sequencing of SARS-CoV-2 allows reconstruction of its transmission history, although this is contingent on sampling. We have analyzed 453 SARS-CoV-2 genomes collected between 20 February and 15 March 2020 from infected patients in Washington State, USA. We find that most SARS-CoV-2 infections sampled during this time derive from a single introduction in late January or early February 2020 which subsequently spread locally before active community surveillance was implemented."

Science: The emergence of SARS-CoV-2 in Europe and North America

"Accurate understanding of the global spread of emerging viruses is critically important for public health responses and for anticipating and preventing future outbreaks. Here, we elucidate when, where and how the earliest sustained SARS-CoV-2 transmission networks became established in Europe and North America. Our results suggest that rapid early interventions successfully prevented early introductions of the virus into Germany and the US from taking hold. Other, later introductions of the virus from China to both Italy and to Washington State founded the earliest sustained European and North America transmission networks. Our analyses demonstrate the effectiveness of public health measures in preventing onward transmission and show that intensive testing and contact tracing could have prevented SARS-CoV-2 from becoming established."

ICYMI

Ann Intern Med: <u>Attitudes Toward a Potential SARS-CoV-2 Vaccine: A Survey of U.S. Adults</u> (posted 04 September 2020)

"Cross-sectional survey, fielded from 16 through 20 April 2020.... Approximately 1000 adults drawn from the AmeriSpeak probability-based research panel, covering approximately 97% of the U.S. household population....

A total of 991 AmeriSpeak panel members responded. Overall, 57.6% of participants (n = 571) intended to be vaccinated, 31.6% (n = 313) were not sure, and 10.8% (n = 107) did not intend to be vaccinated. Factors independently associated with vaccine hesitancy (a response of "no" or "not sure") included younger age, Black race, lower educational attainment, and not having received the influenza vaccine in the prior year. Reasons for vaccine hesitancy included vaccine-specific concerns, a need for more information, antivaccine attitudes or beliefs, and a lack of trust....

This national survey, conducted during the coronavirus pandemic, revealed that approximately 3 in 10 adults were not sure they would accept vaccination and 1 in 10 did not intend to be vaccinated against COVID-19. Targeted and multipronged efforts will be needed to increase acceptance of a COVID-19 vaccine when one becomes available."

BMJ: <u>Drug treatments for covid-19: living systematic review and network meta-analysis</u> (published 30 July 2020; final version 04 September 2020)

"Living systematic review and network meta-analysis.... Randomized clinical trials in which people with suspected, probable, or confirmed covid-19 were randomised to drug treatment or to standard care or placebo. Pairs of reviewers independently screened potentially eligible articles.

5 trials with 16 588 patients met inclusion criteria; 12 (24.3%) trials and 6853 (41.3%) patients are new from the previous iteration. Twenty-seven randomised controlled trials were included in the analysis performed on 29 July 2020. Compared with standard care, glucocorticoids probably reduce death (risk difference 31 fewer per 1000 patients, 95% credible interval 55 fewer to 5 fewer, moderate certainty), mechanical ventilation (28 fewer per 1000 patients, 45 fewer to 9 fewer, moderate certainty), and duration of hospitalisation (mean difference –1.0 day, –1.4 to –0.6 days moderate certainty). The impact of remdesivir on mortality, mechanical ventilation, and length of hospital stay is uncertain, but it probably reduces duration of symptoms (–2.6 days –4.3 to –0.6 days, moderate certainty) and probably does not substantially increase adverse effects leading to drug discontinuation (3 more per 1000, 7 fewer to 43 more, moderate certainty). Hydroxychloroquine may not reduce risk of death (13 more per 1000, 15 fewer to 43 more, low certainty) or mechanical ventilation (19 more per 1000, 4 fewer to 45 more, moderate certainty). The certainty in effects for all other interventions was low or very low certainty.

Glucocorticoids probably reduce mortality and mechanical ventilation in patients with covid-19 compared with standard care, whereas hydroxychloroquine may not reduce either. The effectiveness of most interventions is uncertain because most of the randomised controlled trials so far have been small and have important limitations."

Selected Literature: Preprints

Preprints are found on preprint servers such as <u>arXiv</u>, <u>bioRxiv</u>, and <u>medRxiv</u>; they are commonly used for biomedical research. Preprints may later be published in peer-reviewed journals.Per medRxiv: "Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

medRxiv: <u>Secondary traumatic stress and burnout in healthcare workers during COVID-19</u> <u>outbreak</u> (posted 14 September 2020)

"Aims: To assess the level of professional burnout and secondary traumatic stress, and to identify potential risk or protective factors among health care workers (HCWs) during the coronavirus disease 2019 (COVID-19) outbreak.

Materials and Methods: This cross-sectional study, based on an online survey, collected demographic data and mental distress outcomes from 184 HCWs from May 1st, 2020, to June,15th, 2020, from 45 different countries. The degree of secondary traumatization was assessed using the Secondary Traumatic Stress Scale (STSS), the degrees of perceived stress and burnout were assessed with Perceived Stress Scale (PSS) and Maslach Burnout

Inventory Human Service Survey (MBI-HSS) respectively. Stepwise multiple regression analysis was performed to identify potential risk and protective factors for STS.

Results: 184 HCWs (M=90; Age mean: 46.45; SD:11.02) completed the survey. A considerable proportion of HCWs had symptoms of secondary traumatic stress (41.3%), emotional exhaustion (56.0%), and depersonalization (48.9%). The prevalence of secondary traumatic stress in frontline HCWs was 47.5% while in HCWs working in other units it was 30.3% (p<.023); additionally, the prevalence of the same outcome was 67.1% for the HCWs exposed to patients' death and 32.9% for those HCWs which were not exposed to the same condition (p<.001). In stepwise multiple regression analysis, perceived stress, emotional exhaustion and exposure to patients' death remained as significant predictors in the final model for secondary traumatic stress (adjusted R2 =0.537, p<0.001).

Conclusions: During the current COVID-19 pandemic, HCWs facing patients' physical pain, psychological suffering, and death are more likely to develop secondary traumatization."

medRxiv: <u>Slight reduction in SARS-CoV-2 exposure viral load due to masking results in a significant reduction in transmission with widespread implementation</u> (posted 14 September 2020)

"Masks are a vital tool for limiting SARS-CoV-2 spread in the population. Here we utilize a mathematical model to assess the impact of masking on transmission within individual transmission pairs and at the population level. Our model quantitatively links mask efficacy to reductions in viral load and subsequent transmission risk. Our results reinforce that the use of masks by both a potential transmitter and exposed person substantially reduces the probability of successful transmission, even if masks only lower exposure viral load by ~50%. Slight increases in masking relative to current levels would reduce the reproductive number substantially below 1, particularly if implemented comprehensively in potential superspreader environments. Our model predicts that moderately efficacious masks that reduce transmission risk by 50% will lower exposure viral load 10-fold among people who do get infected, potentially limiting infection severity. Because peak viral load tends to occur presymptomatically, we also identify that antiviral therapy targeting symptomatic individuals is unlikely to impact transmission risk. Instead, antiviral therapy is only effective for this indication as post-exposure prophylaxis, specifically if given to ~50% of newly infected people within 3 days of an exposure. These results highlight the primacy of masking relative to other biomedical interventions under consideration for limiting the extent of the COVID-19 pandemic prior to widespread implementation of a vaccine."

medRxiv: <u>Environment influences SARS-CoV-2 transmission in the absence of non-pharmaceutical interventions</u> (posted 14 September 2020)

"As COVID-19 continues to spread across the world, it is increasingly important to understand the factors that influence its transmission. Seasonal variation driven by responses to changing environment has been shown to affect the transmission intensity of

several coronaviruses. However, the impact of the environment on SARS-CoV-2 remains largely unknown, and thus seasonal variation remains a source of uncertainty in forecasts of SARS-CoV-2 transmission. Here we address this issue by assessing the association of temperature, humidity, UV radiation, and population density with estimates of transmission rate (R). Using data from the United States of America, we explore correlates of transmission across USA states using comparative regression and integrative epidemiological modelling. We find that policy intervention ('lockdown') and reductions in individuals' mobility are the major predictors of SARS-CoV-2 transmission rates, but in their absence lower temperatures and higher population densities are correlated with increased SARS-CoV-2 transmission. Our results show that summer weather cannot be considered a substitute for mitigation policies, but that lower autumn and winter temperatures may lead to an increase in transmission intensity in the absence of policy interventions or behavioural changes. We outline how this information may improve the forecasting of SARS-CoV-2, its future seasonal dynamics, and inform intervention policies."

medRxiv: <u>Racial disparities in COVID-19 mortality are driven by unequal infection risks</u> (posted 11 September 2020)

"Background. As of August 5, 2020, there were more than 4.8M confirmed and probable cases and 159K deaths attributable to SARS-CoV-2 in the United States, with these numbers undoubtedly reflecting a significant underestimate of the true toll. Geographic, racialethnic, age and socioeconomic disparities in exposure and mortality are key features of the first and second wave of the U.S. COVID-19 epidemic.

Methods. We used individual-level COVID-19 incidence and mortality data from the U.S. state of Michigan to estimate age-specific incidence and mortality rates by race/ethnic group. Data were analyzed using hierarchical Bayesian regression models, and model results were validated using posterior predictive checks.

Findings. In crude and age-standardized analyses we found rates of incidence and mortality more than twice as high than Whites for all groups other than Native Americans. Of these, Blacks experienced the greatest burden of confirmed and probable COVID-19 infection (Age- standardized incidence = 1,644/100,000 population) and mortality (age-standardized mortality rate 251/100,000). These rates reflect large disparities, as Blacks experienced age-standardized incidence and mortality rates 5.6 (95% CI = 5.5, 5.7) and 6.9 (6.5, 7.3) times higher than Whites, respectively. We also found that the bulk of the disparity in mortality between Blacks and Whites is driven by dramatically higher rates of COVID-19 infection across all age groups, particularly among older adults, rather than age-specific variation in case-fatality rates.

Interpretation. This work suggests that well-documented racial disparities in COVID-19 mortality in hard-hit settings, such as the U.S. state of Michigan, are driven primarily by variation in household, community and workplace exposure rather than case-fatality rates."

medRxiv: <u>Quantifying proximity, confinement, and interventions in disease outbreaks: a decision support framework for air-transported pathogens</u> (posted 10 September 2020)

"The inability to communicate how infectious diseases are transmitted in human environments has triggered avoidance of interactions during the COVID-19 pandemic. We define a metric, Effective ReBreathed Volume (ERBV), that encapsulates how infectious pathogens transport in air. This measure distinguishes environmental transport from other factors in the chain of infection, thus allowing quantitative comparisons of the riskiness of different situations for any pathogens transported in air, including SARS-CoV-2. Particle size is a key factor in transport, removal onto surfaces, and elimination by mitigation measures, so ERBV is presented for a range of exhaled particle diameters: 1 μm, 10 μm, and 100 μm. Pathogen transport is enhanced by two separate but interacting effects: proximity and confinement. Confinement in enclosed spaces overwhelms proximity after 10-15 minutes for all but the largest particles. Therefore, we review plausible strategies to reduce the confinement effect. Changes in standard ventilation and filtration can reduce person-toperson transport of 1-µm particles (ERBV1) by 13-85% in residential and commercial situations. Deposition to surfaces competes with intentional removal for 10-μm and 100-μm particles, so the same interventions reduce ERBV10 by only 3-50%, and ERBV100 is unaffected. Determining transmission modes is critical to identify intervention effectiveness, and would be accelerated with prior knowledge of ERBV. When judiciously selected, the interventions examined can provide substantial reduction in risk, and the conditions for selection are identified. The framework of size-dependent ERBV supports analysis and mitigation decisions in an emerging situation, even before other infectious parameters are well known."

News in Brief

A new milestone: as of Friday, 18 September, COVID-19 has caused over 30 million total cases and almost 947,000 deaths globally. The US – which makes up 4.25% of the world's population – accounts for 22% of cases and 20% of deaths globally (JHU CSSE; US Census).

Around 14% of COVID-19 cases are in healthcare workers; HCWs cases can be as high as 35% in some countries (WHO).





"We should have treated COVID as a natural disaster, not a public health emergency" (Slate).

Six months into the pandemic and shortages of N95 masks persist (NPR).

"Why coming up with effective interventions to address COVID-19 is so hard" (FiveThirtyEight).

Transmission and Exposure

The 'superspreader' event that was focused around a wedding in Maine has been linked to 7 deaths – none of whom attended (WaPo).

Wearing eyeglasses daily may offer a tiny benefit against getting infected with the coronavirus, according to a small observational study in China (Medpage; see the brief report in JAMA
Ophthalmol).

"Making gyms safer: why the virus is less likely to spread there than in a bar" (KHN).

Long read: "The Carnival Cruise Ship That Spread Coronavirus Around the World" (Bloomberg)

Testing and Emerging Treatments

"One-in-seven U.S. adults (14%) say they have tested positive for COVID-19 or are 'pretty sure' they have had it despite not receiving an official diagnosis, according to a Pew Research Center survey" (Pew).

"Fast coronavirus tests: what they can and can't do" (Nature).

According to new data, an antibody drug from Eli Lilly may help patients get rid of the coronavirus in their system faster (<u>STAT</u>).

Baricitinib in combination with remdesivir is also showing promise as a potential therapy for COVID-19 by reducing time to recovery (Lilly).

The <u>UK RECOVERY trial</u> will add REGN-COV2 – a monoclonal antibody designed in the lab – and compare to standard care (<u>Reuters</u>).

Vaccines

"A COVID-19 vaccine may be only 50% effective. Is that good enough?" (NPR)

The world's largest vaccine manufacturer warns than there may not be enough COVID-19 vaccine for everyone until 2024 (FT).

AstraZeneca's COVID-19 vaccine trial – which was paused last week after a participant had a serious adverse reaction (symptoms were consistent with transverse myelitis) – has resumed (<u>STAT</u>). The University of Oxford suggested that the adverse event was not caused by the vaccine (<u>Reuters</u>).

Pfizer and BioNTech have increased enrollment to 44,000 for the Phase 3 trial of their coronavirus vaccine (<u>STAT</u>). The vaccine could be ready by the end of year, according to Pfizer's CEO (<u>CNBC</u>).

Enrollment updates and the study protocol for the third coronavirus vaccine in Phase 3 trials have been posted (Moderna). Moderna's CEO says they expect to know if the vaccine works sometime in November (December if the infection rate slows down), and could deliver doses early next year (Boston Globe).

The race to develop a vaccine is highlighting the growing role in medical research by China's military (Nature).

Having prisoners in COVID-19 vaccine trials could pose an ethical dilemma, but the benefits could be greater (<u>Science</u>).

Childhood vaccinations are threatened again – this time, it's because schools are moving online and staying up to date is getting harder to enforce (KHN).

Risk Factors and Ripple Effects

Industrial pollution is correlated with increased coronavirus deaths (<u>ProPublica</u>; peer-reviewed article at <u>Environ Res Lett</u>).

Various studies from around the world have reported a dramatic rise in stillbirths during the pandemic (Nature).

We are just starting to figure out why COVID-19 can damage the brain and cause neurological problems (Nature).

And it's not just the brain at risk; scientists are trying to understand how the coronavirus affects the heart and cause long-term damage (<u>Science</u>).

Long read: "The Other Way Covid Will Kill: Hunger" (NYT).

State of the Biomedical Literature

"A controversial guideline saying people without Covid-19 symptoms didn't need to get tested for the virus came from H.H.S. officials and skipped the C.D.C.'s scientific review process" (NYT).

Michael Caputo, the spokesperson for HHS who does not have a medical or scientific background, demanded and got the right to review and suggest wording for the weekly reports by the CDC published in *MMWR* (<u>Politico</u>).

During a Senate hearing, CDC Director Robert Redfield asserted the independent integrity of *MMWR* and stated that the agency has not be compromised by political influences (Medpage).

Something a bit shocking that we can't blame on the pandemic: "Researchers have identified dozens of open-access journals that went offline between 2000 and 2019, and hundreds more that could be at risk" (Nature; preprint at arXiv).

If you think the scientific literature is getting harder to read and filled with acronyms, you aren't alone (<u>Nature Index</u>; see also this article from <u>eLife</u>).

A study of corresponding authors on preprint servers before and during the pandemic suggests the gender gap is increasing (JAMA Netw Open).

Other Infectious Diseases and Outbreaks

Scientists have developed a \$1 point-of-care test for Ebola and Lassa viruses (MSN).

Speaking of Ebola, the DRC outbreak is now at 123 cases with 50 deaths (WHOAFRO).

On the upside, influenza activity is lower than expected for this time of year globally (<u>WHO</u>; see also this article from <u>MMWR</u>).

If you want to avoid a foodborne outbreak, you should probably stay away from romaine lettuce (<u>Emerg Infect Dis</u>; bonus: CME available!)

Thanks, Coronavirus

The pandemic has impacted the cost of living in unexpected ways; folks are spending more on groceries and less on gas (NPR), along with buying more furniture, electronics, and clothes (NPR).

That might explain why so many things are sold out; well, that and because issues with supply chain disruptions, manufacturing woes, labor crises, and other bottlenecks. Basically, "the pandemic broke online shopping" (Atlantic).

Finally, here is a comprehensive guide to COVID-19 etiquette (aka 'covidiquette') to help you navigate all the changes to social practices and norms due to the pandemic (<u>WaPo</u>).

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